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56496

From: Ozga, Brett
Sent: Tuesday, December 11, 2001 10:11 AM
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Subject: 09/631709

Please search 09/631709.

Thank you,

Brett Ozga
CM1 11b01 or 11d14

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Location:	AA Sequences:	DIALOG:
Date Picked Up: 12/13/01	Structures:	Questel/Orbit:
Date Completed: 12/14/01	Bibliographic:	DRLink:
Searcher Prep/Review:	Litigation:	Lexis/Nexis:
Clerical:	Full text:	Sequence Sys.: 03
Online time:	Patent Family:	WWW/Internet:
	Other:	Other (specify):

DETAILED DESCRIPTION - The method comprises:

(a) selecting an alpha -2,3 sialyltransferase compatible with a fucosylated oligosaccharide having a fucose group in the non-reducing penultimate saccharide position;

(b) selecting a CMP-sialic acid or its analog which is compatible with the sialyltransferase; and

(c) contacting the CMP-sialic acid or its analog with a fucosylated oligosaccharide of formula , in the presence of the sialyltransferase under conditions where the sialic acid or its analog is transferred from the CMP-sialic acid or its analog to the non-reducing sugar terminus of the fucosylated oligosaccharide to form the alpha -2,3 sialylated fucosylated oligosaccharide containing a sialic acid or its analog.

R1 and R2 = saccharide residue and R1 and R2 together represent an acceptor for the selected sialyltransferase;

n = 0-(about)10;

Y = O, NH or S; and

R3 = H, protein, lipid or aglycon moiety having at least 1 C atom.

INDEPENDENT CLAIMS are also included for the following:

(1) the enzymatic synthesis of a fucosylated and alpha -2,3 sialylated oligosaccharide comprising:

(a) selecting an alpha -2,3 sialyltransferase capable of sialylating an oligosaccharide having a fucose group in the non-reducing penultimate saccharide position;

(b) selecting a fucosyltransfease;

(c) selecting a CMP-sialic acid or its analog which is compatible with the sialyltransferase;

(d) selecting a **GDP-fucose** or its analog which is compatible with the fucosyltransferase; and

(e) contacting the CMP-sialic acid or its analog and the **GDP -fucose** with an oligosaccharide of formula R1-R2-(saccharide)n-Y-R3, in the presence of the sialyltransferase and the fucosyltransferase, under conditions where the sialic acid or its analog and the fucose or its analog are transferred from the CMP-sialic acid or its analog, and the **GDP-fucose** or its analog, to the non-reducing sugar terminus of the oligosaccharide, to form the alpha -2,3 sialylated fucosylated oligosaccharide, R1 and R2 representing an acceptor for the selected sialyltransferase and the selected fucosyltransferase; and

(2) a method for determining the non-reducing terminus structure of an unknown oligosaccharide acceptor comprising

(a) contacting the oligosaccharide acceptor with a sialyltransferase, which is not capable of sialylating a non-reducing terminus of an oligosaccharide having a fucose group in the non-reducing penultimate saccharide position, and determining whether the oligosaccharide was sialylated;

(b) contacting the oligosaccharide with an alpha -2,3 sialyltransferase which is capable of sialylating a non-reducing terminus of an oligosaccharide having a fucose group in the non-reducing penultimate saccharide position and determining whether the oligosaccharide was sialylated; and

(c) comparing the results to determine whether the non-reducing terminus was fucosylated.

USE - The method is useful for the production of sialylated oligosaccharides (claimed), a cell-mediated antigen immune response suppressant.

Dwg.0/0

L8 ANSWER 4 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 2000-224366 [19] WPIDS
DNC C2000-068535
TI New crystalline **Guanosine diphosphate-fucose** synthetase for identifying agonist and antagonist of its human homolog and for the design of immunosuppressants that acts by blocking selectin mediated cell adhesion.
DC B04 D16
IN SOMERS, W S; STAHL, M L; SULLIVAN, F X
PA (AMHP) AMERICAN HOME PROD CORP
CYC 81
PI WO 2000009744 A1 20000224 (200019)* EN 56p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9954836 A 20000306 (200030)
ADT WO 2000009744 A1 WO 1999-US18441 19990813; AU 9954836 A AU 1999-54836 19990813
FDT AU 9954836 A Based on WO 200009744
PRAI US 1998-96452 19980813
AB WO 200009744 A UPAB: 20000419
NOVELTY - A crystalline **GDP-fucose** synthetase (GFS), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a crystalline composition (I) comprising GFS in association with a chemical species;
(2) a model (II) of the GFS structure comprising a data set embodying the structure of the crystalline GFS;
(3) a computer system, comprising computer hardware (II);
(4) identification of a species which is an agonist/antagonist of GFS or human homolog of GFS (FX) by studying the interaction of candidate species with (II);
(5) a species identified by the method of (4);
(6) a process of identifying a substance which inhibits GFS activity or binding, comprising determining the interaction between a candidate substance and (II);
(7) identification of inhibitors of GFS or human FX protein activity or binding by rational drug design comprises designing a potential inhibitor that will form non-covalent bonds with one or more amino acids in the GFS sequence based on the crystal structure coordinates of crystalline GFS, and synthesizing and determining potential inhibitor of GFS or human FX protein;
(8) an agonist or antagonist identified by the method of (7)
(9) a substance identified by (6);
(10) a method of identifying a species which is an agonist or antagonist of human FX protein activity or binding, comprising studying the interaction of candidate species with (II), and selecting a species which is predicted to act as an agonist or antagonist;
(11) a species identified by the method of (10);

(12) a process of identifying a substance which inhibits human FX protein activity or binding, comprising determining the interaction between a candidate substance and (II);

(13) a method of identifying inhibitors of human FX protein activity by rational drug design comprising, designing a potential inhibitor which will form non-covalent bonds with one or more amino acids in the GFS sequence based upon the crystal structure co-ordinates of (I), synthesizing the inhibitor, and determining whether the potential inhibitor inhibits the activity of the human FX protein;

(14) am agonist or antagonist identified by (13); and

(15) a substance identified by (12).

USE - The crystalline structure of GFS derived from Escherichia coli is useful for identifying its agonist and antagonists (claimed) and is useful for the design of inhibitors of the human GFS which ultimately could lead to the design of immunosuppressants that act by blocking selectin mediated cell adhesion.

Dwg.0/8

L8 ANSWER 5 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-493492 [41] WPIDS
CR 1998-206571 [18]; 1999-152775 [13]
DNC C1999-144489
TI Composition containing an antibody that binds to GDP-D-mannose 4,6-dehydratase useful as a diagnostic tool.
DC B04 D16
IN KRIZ, R; KUMAR, R; SULLIVAN, F
PA (GEMY) GENETICS INST INC
CYC 1
PI US 5942228 A 19990824 (199941)* 9p
ADT US 5942228 A Div ex US 1996-753233 19961122, Div ex US 1997-984246 19971203, US 1998-149674 19980909
FDT US 5942228 A Div ex US 5728568, Div ex US 5869307
PRAI US 1996-753233 19961122; US 1997-984246 19971203; US 1998-149674 19980909
AB US 5942228 A UPAB: 19991011
NOVELTY - Composition containing an antibody which binds to human GDP-D-mannose 4,6-dehydratase of amino acid sequence (I), (II) and a fragment of (I) or (II) with GDP-D-mannose 4,6-dehydratase activity which are substantially free from association with other proteins is new.

USE - The antibodies can also be used as diagnostic tools or in research to study enzyme activity and disease states relating to GDP-D-mannose 4,6-dehydratase.

Dwg.0/0

L8 ANSWER 6 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-417977 [35] WPIDS
CR 1996-477141 [47]; 1996-477142 [47]
DNC C1999-122721
TI 'One-pot' enzymatic manufacture of oligosaccharides for use as antigens, diagnostic agents or therapeutics.
DC B04 D16
IN BAYER, R J; DEFREES, S; RATCLIFFE, M
PA (CYTE-N) CYTEL CORP
CYC 1
PI US 5922577 A 19990713 (199935)* 26p
ADT US 5922577 A CIP of US 1995-419659 19950411, CIP of US 1995-419669 19950411, US 1996-628545 19960410

FDT US 5922577 A CIP of US 5728554
PRAI US 1996-628545 19960410; US 1995-419659 19950411; US 1995-419669 19950411
AB US 5922577 A UPAB: 19990902
NOVELTY - Formation of glycosidic linkages (I) using a glycosyl transferase, a donor substrate, an acceptor sugar, and a divalent metal cation, is new.
DETAILED DESCRIPTION - Formation of (I) comprises:
(a) mixing at least 1 glycol transferase, a donor substrate, an acceptor sugar and a divalent metal cation (2-75 mM); and
(b) following the initiation of a reaction forming (I), restoring or maintaining the concentration of the divalent metal cation at 1-75 mM without the interruption of the linkage-forming reaction.
INDEPENDENT CLAIMS are also included for the following:
(1) a method for the preparation of a compound of formula (II) comprising: (a) treating GlcN(R') beta (1-->3)Gal beta -OR with a galactosyltransferase in the presence of UDP-galactose to form Gal beta (1-->4)GlcN(R') beta (1-->3)Gal beta -OR; (b) treating the product of (a) with alpha (2,3)sialyltransferase in the presence of a CMP derivative of sialic acid to form NeuAc alpha (2-->3)Gal beta (1-->4)(Fuc alpha 1-->3)GlcN(R') beta (1-->3)-OR; and (c) fucosylating the product of (b) to form (II); where the galactosylating and sialylating steps are conducting in a reaction medium comprising a divalent metal cation added to achieve or maintain a cation concentration of 1-75 mM; and
(2) a method for the synthesis of CMP-NeuAc comprising: (a) mixing CMP-NeuAc synthetase, sialic acid, CTP and a 2-75 mM of a soluble divalent metal cation; and (b) following the initiation of a linkage forming step restoring or maintaining the concentration of the divalent metal cation at 1-75 mM without the interruption of the linkage-forming reaction.
NeuAc alpha (2-->3)Gal beta (1-->4)(Fuc alpha 1-->3)GlcN(R') beta (1-->3)Gal beta -OR (II)
R = H, a saccharide, an oligosaccharide, or an aglycon group (at least 1C), preferably an ethyl group;
R' = an acetyl or preferably an allyloxycarbonyl group.
USE - The methods provide for the enzymatic synthesis of oligosaccharides. The compound manufactured by the process may be useful as antigens, diagnostic agents or therapeutics.
ADVANTAGE - Oligosaccharides may be manufactured in a single vessel using readily available starting materials
DESCRIPTION OF DRAWING(S) - The diagram shows an illustrative galactosyl transferase cycle.
Dwg.2/11

L8 ANSWER 7 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-395174 [33] WPIDS
DNC C1999-116188
TI A new glycosyltransferase fusion protein useful in the enzymatic synthesis of oligosaccharides.
DC B04 D16
IN GILBERT, M; WAKARCHUK, W W; YOUNG, N M
PA (CANA) NAT RES COUNCIL CANADA
CYC 83
PI WO 9931224 A2 19990624 (199933)* EN 63p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9917457 A 19990705 (199948)
EP 1040186 A2 20001004 (200050) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9931224 A2 WO 1998-CA1180 19981215; AU 9917457 A AU 1999-17457 19981215; EP 1040186 A2 EP 1998-962154 19981215, WO 1998-CA1180 19981215
FDT AU 9917457 A Based on WO 9931224; EP 1040186 A2 Based on WO 9931224
PRAI US 1998-211691 19981214; US 1997-69443 19971215
AB WO 9931224 A UPAB: 19990819
NOVELTY - A nucleic acid (I) encoding a fusion protein that comprises a glycosyltransferase (GT) catalytic domain and a catalytic domain from an accessory enzyme that is involved in formation of a nucleotide sugar which is a saccharide donor for a glycosyltransferase reaction, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an expression vector or host cell which comprises (I);
(2) a fusion polypeptide encoded by (I); and
(3) a method of producing a fusion polypeptide as defined above.
ACTIVITY - None given.
MECHANISM OF ACTION - Glycosyltransferase.
USE - The fusion polypeptide is useful in the enzymatic synthesis of oligosaccharides. The fusion proteins are able to catalyze more than one reaction involved in the enzymatic synthesis. This is useful for the development of therapeutic agents that have specific carbohydrate structures. Carbohydrates are involved in recognition elements on the surface of cells. The fusion protein can be used for the synthesis of both natural carbohydrates and synthetic derivatives with novel properties.
ADVANTAGE - The fusion polypeptide allows two glycosyltransferase reactions in a single vessel, provides improved yields of end products. Additionally, cleanup and disposal of extra solvents and by-products is reduced. The fusion protein can also use directly different donor analogues and various acceptors with a terminal galactose residue.
Dwg.0/4

L8 ANSWER 8 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-350327 [30] WPIDS
DNC C1999-103462
TI New alpha-1,2-fucosyltransferase - useful as a glycosyltransferase.
DC B04 D16
PA (NODA) ZH NODA SANGYO KAGAKU KENKYUSHO
CYC 1
PI JP 11127866 A 19990518 (199930)* 10p
ADT JP 11127866 A JP 1997-316622 19971104
PRAI JP 1997-316622 19971104
AB JP 11127866 A UPAB: 19990802
A new alpha-1,2-fucosyltransferase has the following properties: (1) Action: It transfers the fucose of **GDP**-beta-L-**fucose** to the 2-OH of the galactose of phenyl-beta-D-galactoside to form phenyl-2-O-(alpha-L-fucopyranosyl)-beta-D-galactopyranoside; (2) Substrate

specificity: It reacts specifically with phenyl-beta-D-galactoside, 2-acetamido-2-deoxy-3-O-(beta-D-galactopyranosyl)-D-glucopyranose, 2-acetamido-2-deoxy-4-O-(beta-D-galactopyranosyl)-D-glucopyranose and 2-acetamido-2-deoxy-3-O-(beta-D-galactopyranosyl)-D-galactopyranose and particularly has a high activity to 2-acetamido-2-deoxy-3-O-(beta-D-galactopyranosyl)-D-galactopyranose; (3) Optimum pH range: Near 6; (4) Optimum temperature range: 18 degrees C in Na phosphate buffer (pH 6.1).

Also claimed are: (1) an alpha-1,2-fucosyltransferase gene coding a polypeptide containing a fully defined 367 amino acid sequence given in the specification, or with at least one amino acid added deleted or replaced and retaining the above properties; (2) a recombinant DNA in which the above alpha-1,2-fucosyltransferase gene is recombined to a vector DNA; and (3) a method for the preparation of alpha-1,2-fucosyltransferase in which a cell containing the above recombinant DNA is cultured in a medium and alpha-1,2-fucosyltransferase is collected from the culture.

USE - As a glycosyltransferase.

ADVANTAGE - The new alpha-1,2-fucosyltransferase is excellent in low temperature reactivity and high in substrate specificity and is useful as a glycosyltransferase.

Dwg.0/4

L8 ANSWER 9 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-520127 [44] WPIDS
DNC C1998-156121
TI DNA encoding fucosyltransferase enzyme - useful for producing recombinant enzyme and genotyping person as secretor or nonsecretor.
DC B04 D16
IN GIORGI, D; KELLY, R J; LENNON, G; LOWE, J B; ROUQUIER, S
PA (GIOR-I) GIORGI D; (KELL-I) KELLY R J; (LENN-I) LENNON G; (LOWE-I) LOWE J B; (ROUQ-I) ROUQUIER S
CYC 1
PI US 5807732 A 19980915 (199844)* 55p
ADT US 5807732 A US 1995-395800 19950228
PRAI US 1995-395800 19950228
AB US 5807732 A UPAB: 19981104
DNA encoding fucosyltransferase comprises a partial DNA sequence selected from nucleotides 1-2115, 148-1092, or 120-1092 of a defined sequence of 2115 bp as given in the specification.

Also claimed are:
(1) a plasmid containing the above DNA, and
(2) a transformed cell containing the plasmid of (1).

USE - The DNA is useful for producing recombinant human **GDP-L-fucose**: beta -D-galactoside 2- alpha -L-fucosyltransferase which can be used for genotyping an individual as a secretor or nonsecretor as it is known that nonsecretors homozygous for a mutant allele of the **GDP-L-fucose**: beta -D-galactoside 2-alpha -L-fucosyltransferase gene (FUT2) that has a stop codon in the position corresponding to amino acid 143.

Dwg.0/11

L8 ANSWER 10 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-261013 [23] WPIDS
DNC C1998-081003
TI Purification of carbohydrate(s) by nano filtration or reverse osmosis

membrane - e.g. oligo saccharide(s) obtained by enzymatic synthesis.
DC A23 A88 B03 B04 D16 D17 E11 E13 J01
IN DEFREES, S
PA (CYTE-N) CYTEL CORP; (NIOT-N) NIOTH TECH CO LTD
CYC 80
PI WO 9815581 A1 19980416 (199823)* EN 54p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9850816 A 19980505 (199836)
EP 931097 A1 19990728 (199934) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1242776 A 20000126 (200024)
ADT WO 9815581 A1 WO 1997-US18801 19971009; AU 9850816 A AU 1998-50816 19971009; EP 931097 A1 EP 1997-913687 19971009, WO 1997-US18801 19971009; CN 1242776 A CN 1997-199688 19971009
FDT AU 9850816 A Based on WO 9815581; EP 931097 A1 Based on WO 9815581
PRAI US 1996-28226 19961010
AB WO 9815581 A UPAB: 19980610
A contaminant (II) is removed from a feed solution comprising a carbohydrate selected from (i)-(viii) or an enzymatic reaction mixture used to prepare (i)-(viii) by contacting the solution with a nanofiltration or reverse osmosis membrane which retains the carbohydrate and allows (II) to pass through. (i) sialyl lactoside; (ii) sialic acid; (iii) lacto-N-neotetraose (LnNT); (iv) GlcNAc beta 1,3Gal beta 1,4Glc (LNT-2); (v) NeuAc alpha (2 => 3)Gal beta (1 => 4)(Fuc alpha 1 => 3)Glc(R1) beta 1-OR2; or (vi) Gal alpha (1 => 3)Gal beta (1 => 4)Glc(R1) beta -O-R3; (vii) a saccharide as described in US5604207; (viii) a nucleotide or a nucleotide sugar; R1 = OH or NAc; R2 = H, alkoxy, saccharide, oligosaccharide or aglycon group having at least 1C atom; R3 = -(CH2)n-COX; R4 = H, saccharide, oligosaccharide or aglycon group; X = OH, OR4 or -NHNH2; and n = 2-18. The nucleotide sugar is preferably **GDP-fucose**, GDP-mannose, CMP-NeuAc, UDP-glucose, UDP galactose or UDP-N-acetylgalactosamine.

The carbohydrate can be NeuAc alpha 2,3Gal beta 1,4(Fuc alpha 1,3)GlcNAc beta 1,4Gal beta 1-OEt; Gal alpha 1,3Gal beta 1,4GlcNAc beta 1-O-(CH2)5-COOH or alpha 2,3- or alpha 2,6-lactoside. The membrane comprises polyamide or polybenzamide and is selected from e.g. a YK, GE(G-5) or MX07 membrane. GH(G-10), HL or MX07.

ADVANTAGE - (I) is purified using a faster, more efficient and less expensive method than by prior methods, e.g. chromatography.
Dwg.0/0

L8 ANSWER 11 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-206571 [18] WPIDS
CR 1999-152775 [13]; 1999-493492 [41]
DNC C1998-065078
TI GDP-mannose 4,6-dehydratase cDNA - useful for producing recombinant GDP-mannose 4,6-dehydratase.
DC B04 D16
IN KRIZ, R; KUMAR, R; SULLIVAN, F
PA (GEMY) GENETICS INST INC

CYC 1
PI US 5728568 A 19980317 (199818)* 9p
ADT US 5728568 A US 1996-753233 19961122
PRAI US 1996-753233 19961122
AB US 5728568 A UPAB: 19991011
GDP-mannose 4,6-dehydratase (GM 4,6D) cDNA clone has a sequence of 1521 bp
(given in the specification) which encodes a GM 4,6D polypeptide a sequence of 354 amino acids (given in the specification) optionally with a
leader sequence of 18 amino acids.
Also claimed are:
(1) an expression vector containing the cDNA with an expression control sequence, and
(2) a host cell transformed with (1).
USE - The method is useful for producing recombinant GM 4,6D, which can be used:
(a) for converting **GDP**-mannose to **GDP-fucose**, which is useful for preparing fucosylated glycoconjugates such as sialyl Lewis X, and
(b) in screening assays for GM 4,6D inhibitors, which may be useful for treating fucose-mediated conditions, e.g. inflammation, arthritis, transplant rejection, asthma, sepsis, reperfusion injury, stroke and infections.
Dwg.0/0

L8 ANSWER 12 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-512415 [47] WPIDS
CR 1997-512414 [47]
DNC C1997-163524
TI **GDP-fucose** pyrophosphorylase and related coding sequences - useful to synthesise **GDP-fucose** as substrate for producing specific carbohydrate structures, e.g. to study cell surface recognition.
DC B04 C06 D16
IN KETCHAM, C M
PA (CYTE-N) CYTEL CORP
CYC 21
PI WO 9737683 A1 19971016 (199747)* EN 40p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP MX
EP 904101 A1 19990331 (199917) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9737683 A1 WO 1997-US5968 19970410; EP 904101 A1 EP 1997-918558 19970410, WO 1997-US5968 19970410
FDT EP 904101 A1 Based on WO 9737683
PRAI US 1997-831590 19970409; US 1996-15241 19960410
AB WO 9737683 A UPAB: 19971125
Isolated nucleic acid encoding **guanosine** 5-**diphospho**-beta L-**fucose** (**GDP-fucose**) pyrophosphorylase (GDPFPP) is new. Also claimed are: (1) the isolated nucleic acid operably linked to a promoter in a recombinant DNA construct; and (2) a composition
comprising an isolated GDPFPP enzyme encoded by the nucleic acid.
USE - The GDPFPP enzyme is useful for synthesis of carbohydrate molecules of defined structures, e.g. for investigating the role of carbohydrates as recognition elements on cell surfaces. The enzyme is

especially useful in producing donor substrates (e.g. **GDP-fucose**) in reactions of a glycosyl transferase (e.g. fucosyltransferase) with the substrate, an acceptor sugar and a divalent metal cation to allow formation of glycosidic linkages adding a saccharide to a substrate saccharide. The GDPFPP can also be used to produce antibodies or antisera useful to characterise, detect and isolate proteins cross-reacting with the enzyme.
Dwg.0/5

L8 ANSWER 13 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-512414 [47] WPIDS
CR 1997-512415 [47]
DNC C1997-163523
TI Nucleic acids encoding **GDP-fucose** pyro phosphorylase - useful to synthesise specific carbohydrate structures e.g. to investigate role of carbohydrate(s) in cell surface recognition.
DC B04 D16
IN DRAKE, R R; ELBEIN, A D; KETCHAM, C M; PASTUSZAK, I
PA (NEOS-N) NEOSE TECHNOLOGIES INC; (CYTE-N) CYTEL CORP; (KETC-I) KETCHAM C M
CYC 21
PI WO 9737682 A1 19971016 (199747)* EN 33p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP MX
US 6033663 A 20000307 (200019)
ADT WO 9737682 A1 WO 1997-US5876 19970409; US 6033663 A Provisional US 1996-15241 19960410, US 1997-826964 19970409
PRAI US 1996-15241 19960410; US 1997-826964 19970409
AB WO 9737682 A UPAB: 20000419
Isolated nucleic acid encoding **guanosine** 5-**diphospho**-beta **L-fucose** (**GDP-fucose**) pyrophosphorylase (GDPFPP) is new. The specification refers to claimed nucleotide and amino acid sequences, neither of which are given in the specification.
USE - Cells can be genetically engineered to contain the nucleic acids and produce the protein (claimed). GDPFPP enzymes can be used to synthesise carbohydrate molecules of defined structures, useful in investigating the role of carbohydrates as recognition elements on cell surfaces. They are especially useful in producing donor substrates (e.g. **GDP-fucose**) in reactions of a glycosyl transferase (e.g. fucosyltransferase) with the substrate, an acceptor sugar and a divalent metal cation to allow formation of glycosidic linkages adding a saccharide to a substrate saccharide. The proteins can also be used to produce antibodies or antisera useful to characterise, detect and isolate proteins cross-reacting with the protein.
Dwg.0/0

L8 ANSWER 14 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-512249 [47] WPIDS
DNC C1997-163420
TI Isolated and homogeneously purified enzyme L-fucokinase - from pig liver has molecular weight 260 kDa and catalyses phosphorylation of L-fucose but not D-glucose, D-galactose or D-mannose.

DC B04 D16
IN ELBEIN, D A
PA (UYAR-N) UNIV ARKANSAS
CYC 20
PI WO 9733981 A1 19970918 (199747)* EN 38p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9723212 A 19971001 (199805)
ADT WO 9733981 A1 WO 1997-US3771 19970311; AU 9723212 A AU 1997-23212 19970311
FDT AU 9723212 A Based on WO 9733981
PRAI US 1996-596907 19960311
AB WO 9733981 A UPAB: 19971125
Isolated and homogeneously purified enzyme L-fucokinase (I) is new.
Also claimed is polyclonal antiserum recognising (I).
USE - L-fucose is an important component of many animal glycolipids and glycoproteins, and is normally formed from D-mannose by internal oxidation-reduction and epimerisation of GDP-D-mannose to produce **GDP**-L-**fucose**. However, studies have indicated that various tissues, e.g. liver and kidneys can also utilise free L-fucose as a precursor of the L-fucose in glycoproteins. Turnover of these polymers may lead to formation of free L-fucose, so that the tissues contain a specific kinase, L-fucokinase, that can phosphorylate L-fucose to form L-fucose-1-phosphate, allowing re-utilisation of L-fucose.
(I) is useful in the synthesis of large amounts of L-fucose-1-P, radio-labelled fucose-1-P, and **GDP**-L-**fucose**, particularly if amino acid sequences are obtained and the enzyme cloned.
ADVANTAGE - (I) was purified 2500-fold with a recovery of activity of 24%, in contrast to 70-fold purification of a prior art L-fucokinase. Both the prior art enzyme and a previously isolated **GDP**-L-**fucose** pyrophosphorylase had broad sugar substrate specificities, indicating possible contamination with other enzymes, e.g. hexokinase.
In contrast (I) is very specific for L-fucose, the only other sugar that could be phosphorylated (about 40% of the rate with L-fucose) being D-arabinose. (I) also only utilises ATP as the phosphate donor, in contrast to the prior art enzyme which could also use CTP, UTP and GTP.
Dwg.0/8

L8 ANSWER 15 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-258275 [23] WPIDS
DNN N1997-213615 DNC C1997-083414
TI Animal model for Helicobacter pylori infection - comprising transgenic mouse expressing human enzyme promoting intestinal adhesion.
DC B04 D16 S03
IN FALK, P; GORDON, J I
PA (UNIW) UNIV WASHINGTON
CYC 1
PI US 5625124 A 19970429 (199723)* 24p
ADT US 5625124 A US 1994-273411 19940711
PRAI US 1994-273411 19940711
AB US 5625124 A UPAB: 19970606
A transgenic mouse expressing an enzyme in its intestinal epithelial cells (IEC) is claimed, where: the enzyme is human **GDP**-L-**fucose**: beta -D-galactoside 2- alpha -L-fucosyltransferase or

human **GDP-L-fucose**: beta -D-N-acetylglucosamide 3/4-
alpha -L-fucosyltransferase; the enzyme is expressed under the control of an IEC-specific promoter; and Helicobacter pylori adheres to the IEC. Also
claimed are IEC from the mouse, where the IEC are cultured in vitro, express the enzyme and bind H. pylori

USE - The transgenic mouse and intestinal epithelial cells from the mouse are useful as models for screening compounds for the ability to inhibit adhesion of H. pylori to IEC. Screening comprises administering H.
pylori bacteria to the mouse or to cultured IEC from the mouse, determining the number of H. pylori bacteria on the surface of the IEC, administering a test compound, and assaying the IEC to determine if the compound decreased the number of adherent H. pylori bacteria (claimed).
Dwg.0/6

L8 ANSWER 16 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1996-425430 [42] WPIDS
DNC C1996-134108
TI Microbial GDP-mannose-pyro phosphorylase and phospho manno mutase - for prodn. of GDP-mannose and for determn. of pyrophosphate-producing nucleotidyl transferase.
DC B04 D16
IN ELLING, L; KULA, M; RITTER, J E; VERSECK, S
PA (KERJ) FORSCHUNGSZENTRUM JUELICH GMBH
CYC 21
PI WO 9627670 A2 19960912 (199642)* DE 52p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
WO 9627670 A3 19961031 (199651)
DE 19606651 A1 19961205 (199703) 28p
EP 813600 A1 19971229 (199805) DE
R: AT BE CH DE DK ES FI FR GB IE IT LI LU NL PT SE
JP 11500921 W 19990126 (199914) 48p
ADT WO 9627670 A2 WO 1996-DE371 19960301; WO 9627670 A3 WO 1996-DE371 19960301; DE 19606651 A1 DE 1996-19606651 19960223; EP 813600 A1 EP 1996-904730 19960301, WO 1996-DE371 19960301; JP 11500921 W JP 1996-526527
19960301, WO 1996-DE371 19960301
FDT EP 813600 A1 Based on WO 9627670; JP 11500921 W Based on WO 9627670
PRAI DE 1996-19606651 19960223; DE 1995-19507449 19950303; DE 1995-19517093 19950515
AB WO 9627670 A UPAB: 19961021
Mannose, or mannose deriv., specific GDP mannose pyrophosphorylase (A), with a specific activity of at least 2U/mg, isolated from a microorganism (esp. a bacterium), is new.

USE - (A) is used to produce GDP-mannose (an intermediate for **GDP-fucose**) from (II) and GTP. The new assay is used to determine (at levels down to 0.2 mU/ml) PPi-producing nucleotidyl transferases.

ADVANTAGE - Because of its mono-functionality, (A) is suitable for use in continuous, multistep processes over a long period. Recombinant (A)
and (B) can be produced in large quantities (contrast isolation from natural sources).
Dwg.0/16

L8 ANSWER 17 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1995-223192 [29] WPIDS
CR 1990-329230 [44]
DNC C1995-102824
TI Prepn. of sialyl dimeric Le(x) and sialyl Le(x) - useful as for developing anticancer and antiinflammatory vaccines.
DC B03 B04 D16
IN CLAUSEN, H; HAKOMORI, S; NUDELMAN, E; SADOZAI, K K; STROUD, M
PA (BIOM-N) BIOMEMBRANE INST
CYC 1
PI US 5421733 A 19950606 (199529)*
ADT US 5421733 A CIP of US 1989-344628 19890428, US 1991-705671 19910524
PRAI US 1991-705671 19910524; US 1989-344628 19890428
AB US 5421733 A UPAB: 19950727
Prepn. of sialyl dimeric Le(x) (I) with a yield of 70% comprises: (1) preparing a sialylnorhexaosylceramide backbone (II) or a sialylnorhexaosyl- saccharide backbone linked to a carrier mol.; and (2) treating the backbone with an isolated fucosyl-transferase lacking alpha 1-2 activity and **GDP-fucose** to produce a backbone in which the III and V positions are fucosylated through an alpha 1-3 linkage. Also claimed is prepn. of sialyl Le(x) with a yield of 70% by (a) preparing a sialyl nortetraosylceramide backbone (IX) or a sialylnorteraosyl saccharide backbone linked to a carrier mol., and (b) treating the backbone with an isolated fucosyl-transferase lacking alpha-1-2 activity and **GDP-fucose** to produce a backbone in which the III position is fucosylated through an alpha 1-3 linkage.
USE - (I) and (X) are expected to be useful components for developing anti-cancer and anti-inflammatory vaccines.
ADVANTAGE - The process is useful for the synthesis of di- and tri-fucosyl Le(x). Their higher analogues and sialyted forms (such as (I) and (X)) by means of a one-step reaction which results in superior yields, cf. prior art reactions, which involve 50 steps.
Dwg.0/14

L8 ANSWER 18 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1995-135887 [18] WPIDS
DNC C1995-062191
TI New alpha-1,3-fucosyl transferase for analysis and synthesis - transfers fucose to specified galactose-N-acetyl- glucosamine terminal selectively.
DC D16 D17
PA (TAKI) TAKARA SHUZO CO LTD
CYC 1
PI JP 07059561 A 19950307 (199518)* 2p
ADT JP 07059561 A JP 1993-225080 19930819
PRAI JP 1993-225080 19930819
AB JP 07059561 A UPAB: 19950518
Alpha-1,3-fucosyl transferase (I) with the following features is new. (1) action: (I) transfers fucose from **GDP fucose** to a hydroxy gp. at 3'-position of GlCNAc using Gal beta 1-4GlcNAc beta 1-R as a receptor, in order to produce Gal beta 1-4(Fuc alpha 1-3)GlcNAc beta 1-R, R=saccharide residue, (2) substrate specificity (I) does not use Gal beta 1-3GlcNAc beta 1-R as a receptor, (I) does not transfer fucose to a

hydroxy gp. at 2'-position of Gal of Gal beta 1-4GlcNAc beta 1-R or Gal beta 1-3GlcNAc beta 1, and (I) does not use NeuAc alpha 2-3Gal beta 1-4GlcNAc beta 1-R as a receptor; (3) optimum pH: pH7.0; (4) pH stability:
(I) is stable at pH6.0-11.0 at 37 deg.C for 5 hrs., and (5) temp. stability: (I) is stable up to around 45 deg.C for 20 min.
USE/ADVANTAGE - By reacting this enzyme with **GDP-fucose** and a saccharide chain of unknown construction for fucose transfer, non-reducing terminal of the saccharide chain is confirmed to include Gal beta 1-4GlcNAc beta 1- structure. Therefore, the enzyme is useful for analysis, modulation, and synthesis of saccharide chain. Only a
small amount of sample is required for analysis with the enzyme, compared to the conventional methylation analysis and NMR spectrum method.
In an example, calf spleen was ground with a buffer contg. a protease
inhibitor, extracted with buffer contg. 1.4% Triton CF-54 and centrifuged.
The supernatant was chromatographed on DEAE cellulose, eluted with a buffer contg. 0.05% Triton CF-54, 5mM EDTA, and protease inhibitor. Eluate
and non-absorbed fractions were combined further diluted with a buffer contg. 0.1% triton CF-54 and protease inhibitor, chromatographed on S-sepharose and eluted with 0.1-1M NaCl (gradient). Active fractions eluted with 0.3-0.8M NaCl were ultra-filtered, desalted with 'Biogel-P-6DG', chromatographed on GDP agarose and finally eluted with a buffer contg. 0.2mM GDP and 0.4M NaCl to obtain alpha-1,3-fucosyl transferase.
Dwg.0/0

L8 ANSWER 19 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1993-018146 [02] WPIDS
CR 1993-018068 [02]; 1993-018069 [02]; 1993-018145 [02]; 1993-036062 [04];
1993-036063 [04]; 1993-405711 [50]; 1993-405712 [50]
DNC C1993-008333
TI New hexa saccharide cpds. prepn. useful in suppression of immune responses
- by mono-fucosylation and silylation using alpha-(1-3)fucosyl transferase.
DC B03 B04 D16
IN IPPOLITO, R; KASHEM, M A; SMITH, R H; VENOT, A P; HANNA, R; HAQUE, W; IPPOLITO, R M; JIANG, C; NIKRAD, P V; HANNA, H R; SRIVASTAVA, O P; KASHEM,
M; SMITH, R
PA (ALBE-N) ALBERTA RES COUNCIL; (GLYC-N) GLYCOMED INC
CYC 18
PI WO 9222662 A1 19921223 (199302)* EN 80p
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: CA JP
EP 588852 A1 19940330 (199413) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
EP 591254 A1 19940413 (199415) EN 4p
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
EP 591256 A1 19940413 (199415) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
US 5374655 A 19941220 (199505) 30p

JP 06510661 W 19941201 (199507) 30p
JP 06510746 W 19941201 (199507) 38p
EP 643718 A1 19950322 (199516) EN
JP 07502011 W 19950302 (199517)
EP 650492 A1 19950503 (199522) EN
US 5550155 A 19960827 (199640)# 28p

ADT WO 9222662 A1 WO 1992-CA251 19920610; EP 588852 A1 EP 1992-911470 19920609, WO 1992-CA244 19920609; EP 591254 A1 EP 1992-911318 19920609, WO 1992-CA245 19920609; EP 591256 A1 EP 1992-911443 19920610, WO 1992-CA251 19920610; US 5374655 A CIP of US 1991-714161 19910610, CIP of US 1991-771259 19911002, CIP of US 1992-889017 19920526, US 1992-914172 19920714; JP 06510661 W JP 1992-511199 19920610, WO 1992-CA251 19920610; JP 06510746 W JP 1992-511196 19920609, WO 1992-CA245 19920609; EP 643718 A1 EP 1993-914163 19930526, WO 1993-US4995 19930526; JP 07502011 W JP 1992-511195 19920609, WO 1992-CA244 19920609; EP 650492 A1 EP 1993-914105 19930524, WO 1993-US4909 19930524; US 5550155 A CIP of US 1991-714161 19910610, CIP of US 1991-771259 19911002, CIP of US 1992-889017 19920526, Cont of US 1992-914172 19920714, US 1994-323100 19941014

FDT EP 588852 A1 Based on WO 9222301; EP 591254 A1 Based on WO 9222564; EP 591256 A1 Based on WO 9222662; JP 06510661 W Based on WO 9222662; JP 06510746 W Based on WO 9222564; EP 643718 A1 Based on WO 9324506; JP 07502011 W Based on WO 9222301; EP 650492 A1 Based on WO 9324505; US 5550155 A Cont of US 5374655

PRAI US 1992-889017 19920526; US 1991-714161 19910610; US 1991-771259 19911002; US 1992-895930 19920609; US 1992-988254 19921209; US 1992-988518 19921210; US 1994-323100 19941014

AB WO 9222662 A UPAB: 19950328

Prepn. of an oligosaccharide deriv. of formula (I) comprises: (a) preparing a cpd. of formula (II); (b) fucosylating (II) with an alpha(1-3)fucosyltransferase to form a monofucosylated deriv. of formula (III); (c) removing the blocking gp. from (III); and (d) sialylating the resultant cpd. with sialic acid or an analogue of sialic acid using an alpha(2-3)sialyltransferase to give (I). In formulae Xa is a removalbe blocking gp.; R is an aglycone gp, contg. at least one C atom; Y is L-fucose; Z is sialic acid or an analogue; Q is a gp. of formula (i); R1 is H; and X is H.

USE/ADVANTAGE - (I) and (IV) are useful in suppressing mammalian cell-mediated immune responses. This includes responses to an antigen such as DTH responses, inflammatory responses arising from myocardial infarction, virus-induced pneumonia, shock, multiple organ failure, adult respiratory distress syndrome, psoriasis, arthritis, etc. Dosage is 0.5-50 mg/kg administered parenterally. The cpds. can be prepd. by both chemical and enzymatic processes.

Dwg.0/0

Dwg.0/0

L8 ANSWER 20 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 1992-319261 [39] WPIDS

DNN N1992-244240 DNC C1992-141779

TI Measurement of glycosyl transferase activity - comprises reactive substrate of natural oligo-sugar labelled with pyridyl amino gp. and sample sepg. reaction prod. by reverse phase chromatography etc..

DC B04 D16 S03

PA (SRLS-N) SRL KK

CYC 1
PI JP 04222598 A 19920812 (199239)* 5p
ADT JP 04222598 A JP 1990-412907 19901225
PRAI JP 1990-412907 19901225
AB JP 04222598 A UPAB: 19931114
Measurement of glycosyl transferase activity comprises reacting an acceptor substrate of natural oligo sugar labelled with pyridilamino and a sample. After reaction prod. is sepd. by reverse phase chromatography, the acceptor substrate bound to active sugar is measured.
Acceptor substrate is biantenary, triantenary, or tetraantenary alga sugar (esp. an alga sugar having lactosamine). Oligo sugar from transferrin (human.sero-transferrin or bovine lactotransferrin) are prefd.
Cpds. of formula (I) are prefd. The active sugar is CMP-SA for sialic acid transferase, UDP-Gal for galactose transferase, UDP-GalNAc for N-acetylgalactosamine, UDP-GlcNAc for N-acetylgluctosamine, **GDP-fucose** for **fucose** transferase. Oligo sugar from human transferrin of formula (II) labelled pyridilamide (PA) was pref. used as the acceptor substrate.
USE/ADVANTAGE - Glycosyl transferase is the marker of tumour. The new method is rapid and simple method compared with the method using HPLC.
In an example, measurement of fucosyl transferase in human serum comprised 5 microlitre of the phosphate buffer soln. of acceptor substrate (0.08 nM), 10 microlitres of the phosphate buffer soln. of 14C-**GDP**-L-**fucose**, and 50 microlitre, of the phosphate buffer soln. contg. 20 microlitre of human serum, 6.25 microM MnCl2 and 1% BSA in a 96 well microplate and incubated at 37 deg.C for 2 hrs. The reaction was stopped by the heating at 100 deg.C for 3 mins. The prod. was absorbed on the reverse chromatography mini column (Bond Elute) and the column was washed with the phosphate buffer (pH 4.0). It was eluted with methanol and purified. The purified prod. was in the liq. scintillation cocktail and the amt. of acceptor substrate bound to active sugar was measured by liq. scintillation counter.
0/0
Dwg.0/0

L8 ANSWER 21 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1992-269724 [33] WPIDS
DNC C1992-120277
TI Stereoselective prepn. of beta-fuco-pyranosyl-phosphate(s) - by converting tri-protected L-fucose into O-alpha-L-fuco pyranosyl-tri chloro-acetimidate and reacting with acid-free organic phosphate to give beta-anomer.
DC B03
IN HEMBERGER, J; JUNG, K; KINZY, W; SCHMIDT, R R; WEGMANN, B; JUNG, K H; SPANGEHL, B; SPAHNGEHL, B
PA (MERE) MERCK PATENT GMBH
CYC 23
PI DE 4102817 A 19920806 (199233)* 9p
EP 502298 A2 19920909 (199237) DE

R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
AU 9210540 A 19920806 (199239)
CA 2060283 A 19920801 (199242)
JP 04312598 A 19921104 (199251) 8p
CS 9200270 A2 19920812 (199305)
HU 61316 T 19921230 (199306)
ZA 9200720 A 19921230 (199306) 22p
PT 100073 A 19930331 (199317)
TW 206233 A 19930521 (199338)
AU 653383 B 19940929 (199440)
US 5371203 A 19941206 (199503) 9p
EP 502298 A3 19950111 (199538)

ADT DE 4102817 A DE 1991-4102817 19910131; EP 502298 A2 EP 1992-101070 19920123; AU 9210540 A AU 1992-10540 19920129; CA 2060283 A CA 1992-2060283 19920129; JP 04312598 A JP 1992-40712 19920131; CS 9200270 A2
CS 1992-270 19920130; HU 61316 T HU 1992-280 19920130; ZA 9200720 A ZA 1992-720 19920131; PT 100073 A PT 1992-100073 19920130; TW 206233 A TW 1992-101410 19920224; AU 653383 B AU 1992-10540 19920129; US 5371203 A US 1992-828617 19920131; EP 502298 A3 EP 1992-101070 19920123

FDT AU 653383 B Previous Publ. AU 9210540

PRAI DE 1991-4102817 19910131

AB DE 4102817 A UPAB: 19931025

The stereoselective prepn. of beta-L-fucopyranosyl-phosphate derivs. (I) comprises (a) converting L-fucose which is protected on positions 2, 3 and 4 into the corresp. O-(alpha-L-fucopyranosyl) trichloroacetimidate (II); (b) reacting this with an absolute, acid-free organic phosphate (III) of formula PO(OH)(OR2); (c) removing R from the phosphate and the protecting gps. from the fucopyranosyl ring; and (d) isolating (I) as the salt. R = 1-4C alkyl, Ph or benzyl.

The stereoselective prepn. of highly pure **guanosine-diphosphate fucose** (III) comprises (i) converting (I) into a readily soluble salt, (ii) reacting this salt with activated guanosine monophosphate (GMP) and (iii) recovering (III) formed by preparative HPLC using as eluant, a buffer system which is easily evaporated.

USE/ADVANTAGE - (I) can be used in the prepn. of highly pure (III) which can be used in the investigation and prognosis of tumour-associated antigens based on fucosylated glycolipids. Using (I) as the starting material, the prods. are obtd. in good yield with high stereoselectivity using a simple method. (I) can be obtd. in high yields using the invention. Step (a) is stereoselective and gives (II) in good yields. Step (b) is stereoselective, providing there is no acid present in the phosphate used, and gives good yields of (I). The process is relatively simple and uses few reaction steps, e.g. there is no need to separate alpha and beta-aromers. The process can be used on an industrial scale. Dwg.0/0

L8 ANSWER 22 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

AN 1990-372014 [50] WPIDS

DNC C1990-161813

TI Guanosine di phosphate-L-fucose prodn. - by adding di thio-erythritol etc stabilising agent to guanosine di phosphate-D-mannose, etc..

DC B02 D16

PA (SEIT) SUMITOMO SEIKA CHEM CO LTD

CYC 1
PI JP 02268692 A 19901102 (199050)*
ADT JP 02268692 A JP 1989-89565 19890407
PRAI JP 1989-89565 19890407
AB JP 02268692 A UPAB: 19930928
Guanosine diphosphate-L-fucose (GDP-L-Fuc)
is efficiently produced from guanosine diphosphate-D-mannose (GDp-D-Man) by adding dithiothreitol or dithioerythritol as stabilising agent to stabilise enzyme that catalyses transformation reaction from GDP-D-Man to GDP-L-Fuc.
USE/ADVANTAGE - GDP-L-Fuc is important cpd. in immunology as donor of
L-fucosyl gp., important gp. for determn. of blood antigenic types. GDP-L-Fuc is efficiently produced by stabilising enzyme involving formation of GDL-L-Fuc.
0/0

L8 ANSWER 23 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1990-329230 [44] WPIDS
CR 1995-223192 [28]
DNC C1990-142927
TI Synthesis of dimeric lex or di fucosyl y2 cancer antigens - useful as antitumour vaccines and to subside inflammatory processes of rheumatoid arthritis.
DC B04 D16
IN CLAUSEN, H; HAKOMORI, S; NUDELMAN, E; SADOZAI, K; STROUD, M R
PA (BIOM-N) BIOMEMBRANE INST
CYC 15
PI EP 395217 A 19901031 (199044)*
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
CA 2015675 A 19901028 (199104)
JP 04179493 A 19920626 (199232) 19p
ADT EP 395217 A EP 1990-303034 19900321; JP 04179493 A JP 1990-115028 19900427
PRAI US 1989-344628 19890428
AB EP 395217 A UPAB: 19950804
Prepn. of difucosyl Y2 antigen (dimeric Lex) comprises (1) prepg. a lactonorhexaosylceramide backbone or a lactonorhexaosylsaccharide backbone
linked to a carrier molecule and (2) enzymatically fucosylating the backbone at the III3 and V3 positions through an alpha 1-3 linkage.
Also claimed is prepn. of Ley antigen analogues by (1) as above; (2) enzymatically fucosylating the backbone at the terminal beta-Gal through an alpha 1-2 linkage; and (3) enzymatically fucosylating the backbone at one or more positions through an alpha 1-3 linkage, steps(2) and (3) being
conducted simultaneously or any order.
Also claimed is prepn. of alpha 1-2 and/or alpha 1-3 fucosylated lactonor-hexaosylceramide, lactonorhexaosylsaccharide linked to a carrier or their higher analogues by enzymatic fucosylation.
The enzymatic fucosylation of the backbone is pref. performed with alpha 1-3 fucosyltransferase isolated from human colonic adenocarcinoma Colo205 cell line in the presence of **GDP-fucose.**
USE/ADVANTAGE - The process is a highly efficient method for synthesising dimeric Lex antigen (difucosyl Y2). It may also be used to prepare the Y2 antigen, the Z1 antigen, the Z2 antigen and the Z3 antigen (trimeric Lex) (structures provided). The above cpds. are cancer cell

antigens and they may be used as active vaccines for tumours. Dimeric Lex has also been shown to suppress the appearance of inflammatory granulocytes in the bone marrow of rheumatoid arthritis-affected joints.
@(16pp Dwg.No. 0/10)
0/10

L8 ANSWER 24 OF 24 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1982-18788E [10] WPIDS
TI Guanosine di phosphate fucose prodn. - by reacting enzyme of agrobacterium, escherichia or aerobacter microorganism with guanosine di phosphate mannose.
DC B02 D16
PA (ASAH) ASAHI CHEM IND CO LTD
CYC 1
PI JP 57018993 A 19820130 (198210)* 4p
JP 01057959 B 19891208 (199002)
ADT JP 57018993 A JP 1980-92782 19800709
PRAI JP 1980-92782 19800709
AB JP 57018993 A UPAB: 19930915
Guanosine diphosphate fucose (I) is prepd. by reacting enzyme of microorganism of genus Agrobacterium, Echerichia and Aerobacter, with guanosine diphosphate mannose.
Cultivation of microorganism is conducted in medium contg. carbon source (e.g., grape sugar, sucrose, glycerin, molasses, starch, organic acid), nitrogen source (e.g., yeast extract, meat extract, soy bean flour, urea, ammonium salt), and other components necessary for the growth.
(I) is useful as pharmaceutical and biochemical reagent. The method gives (I) efficiently in large amt. and in low cost.

CT Check Tags: Animal; Human; In Vitro; Support, U.S. Gov't, P.H.S.
Chromatography, High Pressure Liquid: MT, methods
Crithidia fasciculata: EN, enzymology
Fucosyltransferases: ME, metabolism
***Guanosine Diphosphate Fucose: BI, biosynthesis**
Guanosine Diphosphate Fucose: CH, chemistry
*Guanosine Diphosphate Sugars: BI, biosynthesis
Guanosine Diphosphate Sugars: CH, chemistry
Kinetics
Leishmania major: EN, enzymology
Nucleotidyltransferases: ME, metabolism
Pentosyltransferases: ME, metabolism
Phosphotransferases (Alcohol Group Acceptor): ME, metabolism
Recombinant Proteins: ME, metabolism
Substrate Specificity
Tritium

L3 ANSWER 6 OF 16 MEDLINE
AN 1999036864 MEDLINE
DN 99036864
TI GDP-4-keto-6-deoxy-D-mannose epimerase/reductase from Escherichia coli, a key enzyme in the biosynthesis of GDP-L-fucose, displays the structural characteristics of the RED protein homology superfamily.
AU Rizzi M; Tonetti M; Vigevani P; Sturla L; Bisso A; Flora A D; Bordo D; Bolognesi M
CS Dipartimento di Scienza e Tecnologia del Farmaco Universita del Piemonte Orientale "A.Avogadro" Viale Ferrucci 33-28100 Novara, Italy.
SO STRUCTURE, (1998 Nov 15) 6 (11) 1453-65.
Journal code: B31. ISSN: 0969-2126.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS PDB-1BWS; PDB-1RBWSSF
EM 199903
EW 19990301
AB BACKGROUND: The process of guanosine 5'-diphosphate L-fucose (GDP-L-fucose) biosynthesis is conserved throughout evolution from prokaryotes to man. In animals, GDP-L-fucose is the substrate of fucosyltransferases that participate in the biosynthesis and remodeling of glycoconjugates, including ABH blood group and Lewis-system antigens. The 'de novo' pathway of GDP-L-fucose biosynthesis from GDP-D-mannose involves a GDP-D-mannose 4,6 dehydratase (GMD) and a GDP-4-keto-6-deoxy-D-mannose epimerase/reductase (GMER). Neither of the catalytic mechanisms nor the three-dimensional structures of the two enzymes has been elucidated yet. The severe leukocyte adhesion deficiency (LAD) type II genetic syndrome is known to result from deficiencies in this de novo pathway. RESULTS: The crystal structures of apo- and holo-GMER have been determined at 2.1 A and 2.2 A resolution, respectively. Each subunit of the homodimeric (2 x 34 kDa) enzyme is composed of two domains. The N-terminal domain, a six-stranded Rossmann fold, binds NADP+; the C-terminal domain (about 100 residues) displays an alpha/beta topology. NADP+ interacts with residues Arg12 and Arg36 at the adenylic ribose phosphate; moreover, a protein loop

based on the Gly-X-X-Gly-X-X-Gly motif (where X is any amino acid) stabilizes binding of the coenzyme diphosphate bridge. The nicotinamide and the connected ribose ring are located close to residues Ser107, Tyr136
and Lys140, the putative GMER active-site center. CONCLUSIONS: The GMER fold is reminiscent of that observed for UDP-galactose epimerase (UGE) from Escherichia coli. Consideration of the enzyme fold and of its main structural features allows assignment of GMER to the reductase-epimerase-dehydrogenase (RED) enzyme homology superfamily, to which short-chain dehydrogenase/reductases (SDRs) also belong. The location of the NADP+ nicotinamide ring at an interdomain cleft is compatible with substrate binding in the C-terminal domain.

CT Check Tags: Human; Support, Non-U.S. Gov't
Amino Acid Sequence
Binding Sites
Carbohydrate Epimerases: CH, chemistry
*Carbohydrate Epimerases: ME, metabolism
Crystallography, X-Ray
Dimerization
*Escherichia coli: EN, enzymology
***Guanosine Diphosphate Fucose: BI, biosynthesis**
Models, Molecular
Molecular Sequence Data
NADP: ME, metabolism
Protein Conformation
Protein Folding
Sequence Homology, Amino Acid
Sugar Alcohol Dehydrogenases: CH, chemistry
*Sugar Alcohol Dehydrogenases: ME, metabolism

L3 ANSWER 7 OF 16 MEDLINE
AN 1998282279 MEDLINE
DN 98282279
TI Leukocyte Adhesion Deficiency Type II is a generalized defect of de novo GDP-fucose biosynthesis. Endothelial cell fucosylation is not required for
neutrophil rolling on human nonlymphoid endothelium.
AU Karsan A; Cornejo C J; Winn R K; Schwartz B R; Way W; Lannir N; Gershoni-Baruch R; Etzioni A; Ochs H D; Harlan J M
CS Department of Pathology and Laboratory Medicine, University of British Columbia and St. Paul's Hospital, Vancouver, British Columbia, Canada V6Z 1Y6.. akarsan@prl.pulmonary.ubc.ca
NC HL18645 (NHLBI)
GM 42686 (NIGMS)
HL30541 (NHLBI)
SO JOURNAL OF CLINICAL INVESTIGATION, (1998 Jun 1) 101 (11) 2438-45.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199809
EW 19980901
AB Leukocyte Adhesion Deficiency Type II (LAD II) is a recently described syndrome and the two patients with this defect lack fucosylated glycoconjugates. These glycoconjugates include the selectin ligand, sialyl

Specifically, purified FX apparently catalyzes a combined epimerase and NADPH-dependent reductase reaction, converting GDP-4-keto-6-D-deoxymannose to GDP-L-fucose. This is the substrate of several fucosyltransferases involved in the correct expression of many glyco conjugates, including blood groups and developmental antigens.

CC 7-2 (Enzymes)
Section cross-reference(s): 3, 6, 13

ST FX protein activity cDNA sequence human; GDPfucose formation FX protein human; **epimerase reductase** GDPfucose formation FX protein

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(FX; cDNA sequence and synthesis of GDP-L-fucose by the human FX protein, an **epimerase-reductase**)

IT Protein sequences
(of human GDP-4-keto-6-D-deoxymannose **epimerase-reductase**)

IT Deoxyribonucleic acid sequences
(complementary, for human GDP-4-keto-6-D-deoxymannose **epimerase-reductase**)

IT 183450-83-1, Protein FX (human)
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(amino acid sequence; cDNA sequence and synthesis of GDP-L-fucose by the human FX protein, an **epimerase-reductase**)

IT 113756-18-6, GDP-4-keto-6-D-deoxymannose **epimerase-reductase**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(cDNA sequence and synthesis of GDP-L-fucose by the human FX protein, an **epimerase-reductase**)

IT **15839-70-0**, GDP-L-fucose
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(cDNA sequence and synthesis of GDP-L-fucose by the human FX protein, an **epimerase-reductase**)

IT 177823-39-1, GenBank U58766
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; cDNA sequence and synthesis of GDP-L-fucose by the human FX protein, an **epimerase-reductase**)

L16 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1988:145966 HCAPLUS
DOCUMENT NUMBER: 108:145966
TITLE: An **epimerase-reductase** in L-fucose synthesis
AUTHOR(S): Chang, Sulie; Duerr, Barbara; Serif, George
CORPORATE SOURCE: Dep. Biochem., Ohio State Univ., Columbus, OH, 43210-1292, USA
SOURCE: J. Biol. Chem. (1988), 263(4), 1693-7
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 1st committed enzyme in GDP-L-fucose formation from GDP-D-mannose is

GDP-D-mannose 4,6-dehydratase, which forms GDP-4-keto-6-deoxy-D-mannose. The uncertain enzymic steps beyond this point were examd. in this study. Assays were developed for the epimerase and reductase activities which the putative pathway would predict. A protein was isolated from porcine thyroid gland exhibiting homogeneity by several criteria. This single protein, which forms GDP-L-fucose from GDP-4-keto-6-deoxy-D-mannose and NADH, appeared to possess both epimerase and reductase capabilities and may be termed GDP-4-keto-6-deoxy-D-mannose-3,5-epimerase-4-reductase. Anal. on a mol. sieve column using fast protein liq. chromatog. established a mol. wt. of 63,100 for the native enzyme, whereas SDS-PAGE established a subunit mol. wt. of 31,500.

CC 7-2 (Enzymes)
Section cross-reference(s): 13

ST fucose formation **epimerase reductase** thyroid; GDP fucose formation **epimerase reductase**; deoxymannose **epimerase reductase** fucose formation

IT Thyroid gland, composition
(GDP-4-keto-6-deoxymannose **epimerase-reductase** of)

IT 2438-80-4, L-Fucose **15839-70-0**, GDP-L-Fucose
RL: FORM (Formation, nonpreparative)
(formation of, by thyroid gland, purifn. of **epimerase-reductase** in)

not found in other serogroups of the two species. The first of these is common to Ec O111 and Se O:35 (sv Adelaide); the other is found in both Ec
O55 and Se O:50 (sv Greenside). The genes specific for the synthesis of O antigen are generally located in the rfb gene cluster at map position 45 min in Ec and 42 min in Se. The rfb (O antigen) gene cluster of an Ec O111
strain M92 had been cloned earlier and hybridisation analysis suggested that the rfb clusters of Ec M92 and a Se sv Adelaide strain had been acquired separately by the two species since their divergence. We have now
sequenced part of the rfb cluster from Ec M92. We identify two genes of the GDP-colitose pathway, rfbM and rfbK, and show that several other ORFs have similarity to the rfb and cps (capsular polysaccharide) genes. Downstream of this block of genes is an ORF which encodes a protein with predicted transmembrane segments which is presumed to correspond to the rfbX gene. The % G+C values of the Ec M92 rfb sequence are extremely low, indicating that the rfb evolved in a low % G+C species of bacteria before transfer into Ec.

CT Check Tags: Comparative Study; Support, Non-U.S. Gov't
Amino Acid Sequence
Bacterial Proteins: GE, genetics
Base Composition
Base Sequence
*Escherichia coli: GE, genetics
*Genes, Bacterial
Genetic Code
Guanosine Diphosphate Fucose: ME, metabolism
Guanosine Diphosphate Sugars: BI, biosynthesis
Membrane Proteins: GE, genetics
Molecular Sequence Data
*Multigene Family
Nucleotidyltransferases: GE, genetics
*O Antigens
Open Reading Frames
Phosphotransferases (Phosphomutases): GE, genetics
Sequence Analysis, DNA
Sequence Homology

L11 ANSWER 8 OF 9 MEDLINE
AN 88115283 MEDLINE
DN 88115283
TI An epimerase-reductase in L-fucose synthesis.
AU Chang S; Duerr B; Serif G
CS Department of Biochemistry, Ohio State University, Columbus 43210-1292.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1988 Feb 5) 263 (4) 1693-7.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198805
AB The first committed enzyme in GDP-L-fucose formation from GDP-D-**mannose** is GDP-D-**mannose** 4,6-dehydratase, which forms GDP-4-keto-6-deoxy-D-**mannose**. The uncertain enzymatic steps beyond this point were examined in this study. Assays were developed for the epimerase and reductase activities which the putative pathway would

predict. A protein was isolated exhibiting homogeneity by several criteria. This single protein, which forms GDP-L-fucose from GDP-4-keto-6-deoxy-D-**mannose** and NADH, appears to possess both epimerase and reductase capabilities and may be termed GDP-4-keto-6-deoxy-D-**mannose**-3,5-epimerase-4-reductase. Analysis on a molecular sieve column using fast protein liquid chromatography established a molecular weight of 63,100 for the native enzyme, whereas sodium dodecyl sulfate-polyacrylamide gel electrophoresis established a subunit molecular weight of 31,500.

CT Check Tags: Animal; Support, U.S. Gov't, Non-P.H.S.
*Carbohydrate Epimerases: ME, metabolism
***Fucose: BI, biosynthesis**
Guanosine Diphosphate Fucose: ME, metabolism
Kinetics
Molecular Weight
*Rhamnose: AA, analogs & derivatives
Rhamnose: IP, isolation & purification
*Sugar Alcohol Dehydrogenases: ME, metabolism
Swine
Thyroid Gland: EN, enzymology

L11 ANSWER 9 OF 9 MEDLINE
AN 82000645 MEDLINE
DN 82000645
TI Synthesis of L-fucose in thyroid tissue.
AU Overton K; Serif G S
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1981 Jul) 675 (2) 281-4.
Journal code: A0W. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198201
AB A de novo pathway for L-fucose synthesis has been detected in porcine thyroid tissue. This system uses guanosine diphospho-alpha-D **mannose** as a precursor and forms guanosine diphospho-beta-L-fucose as product. The system seems similar to those reported by others to exist in microorganisms and plants in that the first step of the pathway involves a 4-keto sugar nucleotide intermediate. The first enzyme of the pathway, guanosine diphospho-alpha-D-**mannose** oxidoreductase has been purified 57-fold from crude extracts by virtue of its affinity for Blue Sepharose.
CT Check Tags: Animal; Support, U.S. Gov't, Non-P.H.S.
Carbohydrate Dehydrogenases: IP, isolation & purification
Chromatography, Affinity
***Fucose: BI, biosynthesis**
Guanosine Diphosphate Fucose: ME, metabolism
Guanosine Diphosphate Mannose: ME, metabolism
Swine
*Thyroid Gland: ME, metabolism

leukocyte adhesion and trafficking processes. Genetic deletion of these fucosylated structures in the mouse has been a powerful tool to address functional questions about fucosylated glycans. However, successful use of such approaches can be problematic, given the substantial redundancy in the mammalian .alpha.-1,3-fucosyl-transferase and .alpha.-1,2-fucosyltransferase gene families. To circumvent this problem, we have chosen to clone the genetic locus encoding a mammalian GDP-D-mannose-4,6-dehydratase (GMD). This enzyme generates GDP-mannose-4-keto-6-D-deoxymannose from GDP-mannose, which is then converted by the FX protein (GDP-4-keto-6-D-deoxymannose epimerase/GDP-4-keto-6-L-galactose reductase) to GDP-L-fucose. GMD is thus imperative for the synthesis of all fucosylated oligosaccharides. An expression cloning approach and the GMD-deficient CHO host cell line Lec13 were used to generate a population of cDNA mols. enriched in GMD cDNAs. This enriched plasmid population was then screened using a human expressed sequence tag (EST AA065072) with sequence similarity to an Arabidopsis thaliana GMD cDNA. This approach, together with 5'-rapid amplification of cDNA ends, yielded a human cDNA that complements the fucosylation defect in the Lec13 cell line. Northern blot analyses indicate that the GMD transcript is absent in Lec13 cells, confirming the genetic deficiency of this locus in these cells. By contrast, the transcript encoding the FX protein, which forms GDP-L-fucose from the ketosugar intermediate produced by GMD, is present in increased amts. in the Lec13 cells. These results suggest that metabolites generated in this pathway may participate in the transcriptional regulation of the FX protein and possibly the GMD protein. The results also suggest that the genomic structure encoding GMD in Lec13 cells likely has a defect different from a point mutation in the coding region.

CC 7-5 (Enzymes)
Section cross-reference(s): 3, 13, 33

IT **15839-70-0 18186-48-6**
RL: BOC (Biological occurrence); BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
(mol. cloning and expression of GDP-D-mannose-4,6-dehydratase and its role in fucose metab.)

L9 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1992:38516 HCAPLUS
DOCUMENT NUMBER: 116:38516
TITLE: Participation of an endogenous inhibitor of fucosyltransferase activities in the developmental regulation of intestinal fucosylation processes
AUTHOR(S): Ruggiero-Lopez, Daniel; Biol, M. Claire; Louisot, Pierre; Martin, Ambroise
CORPORATE SOURCE: Dep. Gen. Med. Biochem., Lyon-Sud Med. Sch., Oullins, 69921, Fr.
SOURCE: Biochem. J. (1991), 279(3), 801-6
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal

LANGUAGE: English

AB During the rat weaning period (about day 19 after birth) the intestinal maturation is accompanied by a drastic increase in the fucose content of mucosal glycoconjugates, concomitant with an increase in fucosyltransferase activities. The regulation of this fucosylation process appears to be a rather complex phenomenon, which involves several systems controlling fucosyltransferase activity or substrate availability.

An endogenous protein inhibitor of the fucosyltransferase activities displays an opposite developmental pattern to that of fucosyltransferase activities, since its activity is high before weaning and is decreased 5-fold after weaning. Similarly, the GDP-fucose pyrophosphatase activity markedly decreases at weaning. The transformation of GDP-mannose into GDP-fucose increases early, at day 18, preceding the increase in fucosyltransferase activities. Before weaning, and esp. at days 14 and 18, high levels of GDP-4-dehydro-6-deoxymannose, the product of the GDP-mannose 4,6-dehydratase activity, are produced during the transformation of GDP-mannose into GDP-fucose, even in excess of reduced coenzyme. This fact indicates that the 2nd step of the transformation (epimerase-reductase reaction) could be a limiting factor for GDP-fucose availability before weaning, but not after weaning. The inverse relationship between the mucosal fucose content (or the fucosyltransferase activity) and the endogenous protein inhibitor during normal postnatal development supports the hypothesis of a physiol. role for this inhibitor.

CC 13-3 (Mammalian Biochemistry)

IT **15839-70-0**, GDP-Fucose **18186-48-6**
RL: FORM (Formation, nonpreparative)
(formation of, from GDP-mannose by intestine in development)

L9 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1985:3456 HCAPLUS

DOCUMENT NUMBER: 102:3456

TITLE: Study of the conversion of GDP-mannose into GDP-fucose in Nereids: a biochemical marker of oocyte maturation

AUTHOR(S): Bulet, Philippe; Hoflack, Bernard; Porchet, Maurice; Verbert, Andre

CORPORATE SOURCE: Lab. Biol. Anim., Univ. Sci. Tech. Lille, Villeneuve d'Ascq, F-59655, Fr.

SOURCE: Eur. J. Biochem. (1984), 144(2), 255-9
CODEN: EJBCAI; ISSN: 0014-2956

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Homogenates of Perinereis cultrifera oocytes transform GDP-D-mannose into another sugar nucleotide identified as GDP-L-fucose on the basis of UV absorption spectra, chromatog. behavior, and gas-liq. chromatog. coupled to mass spectrometry. This conversion is a multistep reaction as proved by the involvement of 2 intermediates identified as GDP-4-oxo-6-deoxy-D-mannose and GDP-4-oxo-6-deoxy-L-galactose, this latter being reduced by NADPH to give GDP-L-fucose. The enzymic activities responsible for the conversion of GDP-D-mannose into GDP-L-fucose are recovered only in oocytes and not in other coelomic cells (coelomocytes). Max. activity is recovered at a well-defined stage of hormone-controlled oogenesis. Thus, this enzymic system appears as a biochem. marker of oocyte maturation in

P. cultrifera.
CC 12-2 (Nonmammalian Biochemistry)
IT **15839-70-0**
RL: FORM (Formation, nonpreparative)
(formation of, from GDP-mannose by oocyte of polychaete in maturation)
IT **18186-48-6** 93528-34-8
RL: BIOL (Biological study)
(in GDP-fucose formation, by oocyte of polychaete in maturation)

L9 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1980:599923 HCAPLUS
DOCUMENT NUMBER: 93:199923
TITLE: The synthesis of guanosine 5'-diphosphate L-fucose from guanosine 5'-diphosphate 3,5-D-[3H]mannose catalyzed by an enzyme extract from fruits of the flax
AUTHOR(S): Barber, George A.
CORPORATE SOURCE: Dep. Biochem., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Plant Physiol. (1980), 66(2), 326-9
CODEN: PLPHAY; ISSN: 0032-0889
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An enzyme system from fruits of the flax plant is described that catalyzes the synthesis of the sugar nucleotide GDP-L-fucose from GDP-D-mannose with the intermediate formation of GDP-4-oxo-6-deoxy-D-mannose. 3H from 3H2O was incorporated into the L-fucose portion of the sugar nucleotide in the course of the reaction, and 3H at the 3,5-C atoms of the D-mannose moiety of GDP-D-mannose was exchanged with protons in the medium. These results support a mechanism of synthesis analogous to that proposed for the formation of L-rhamnose and other 6-deoxy sugars.
CC 7-3 (Enzymes)
IT **15839-70-0**
RL: FORM (Formation, nonpreparative)
(formation of, by enzyme of flax)
IT **18186-48-6**
RL: BIOL (Biological study)
(in GDP fucose formation from GDP-mannose by enzyme of flax)

D.CA IS NOT A RECOGNIZED COMMAND

COMMAND STACK INTERRUPTED. ENTER "DISPLAY HISTORY"
TO SEE WHICH COMMANDS WERE EXECUTED.

=> d .ca l10 1-3;d .ca l16 1-7

L10 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:961938 HCAPLUS
DOCUMENT NUMBER: 124:108060
TITLE: A putative pathway for perosamine biosynthesis is the first function encoded within the rfb region of Vibrio

cholerae O1
AUTHOR(S): Stroeher, Uwe H.; Karageorgos, Litsa E.; Brown, Melissa H.; Morona, Renato; Manning, Paul A.
CORPORATE SOURCE: Microbial Pathogenesis Unit, Department of Microbiology and Immunology, The University of Adelaide, Adelaide, S.A., 5005, Australia
SOURCE: Gene (1995), 166(1), 33-42
CODEN: GENED6; ISSN: 0378-1119
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The first four genes (rfbA,B,D,E) of the rfb region of Vibrio cholerae O1 are predicted to encode the enzymes required for the biosynthesis of perosamine, which constitutes the backbone structure of the O-antigen of the lipopolysaccharide. Based on homol. to known proteins/protein families, the following functions are predicted: RfbA, phosphomannose isomerase-guanosine diphosphomannose pyrophosphorylase; RfbB, phosphomanno-mutase; RfbD, oxido reductase and RfbE, perosamine synthetase (amino-transferase). Thus, perosamine is synthesized from fructose 6-phosphate via the intermediates mannose 6-phosphate by RfbA, to mannose 1-phosphate by RfbB, to GDP-mannose by RfbA, to GDP-4-keto-6-dideoxymannose by RfbD and to GDP-perosamine by RfbE. This final product would then serve as the substrate for the addn. of the tetronate, which could then be polymd. into the O-antigen for transfer to the lipid A plus core oligosaccharide and export to the cell surface. The organization of these genes are such that one would expect them to be translationally coupled as part of the rfb operon. However, the absence of readily detectable promoter sequences suggests low levels of transcription, in line with other studies. The nucleotide sequence of these genes is absolutely conserved in the two isolates 569B (classical, Inaba) and O17 (El Tor, Ogawa) which were expected to show maximal sequence variation. This suggests very tight constraints on the micro-evolution within these sequences.
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 10
IT 3123-67-9, GDP-mannose 3672-15-9, Mannose 6-phosphate 15978-07-1 **18186-48-6** 172698-73-6
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(perosamine is synthesized in Vibrio cholerae from fructose 6-phosphate to mannose 6-phosphate by RfbA, to mannose 1-phosphate by RfbB, to GDP-mannose by RfbA, to GDP-4-keto-6-dideoxymannose by RfbD and to GDP-perosamine by RfbE)

L10 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:186566 HCAPLUS
DOCUMENT NUMBER: 118:186566
TITLE: Evidence that the enzyme catalyzing the conversion of guanosine diphosphate D-mannose to a 4-keto sugar nucleotide intermediate requires nicotinamide adenine dinucleotide phosphate
AUTHOR(S): Yamamoto, Kenji; Katayama, Isao; Onoda, Yukiko; Inami, Masaki; Kumagai, Hidehiko; Tochikura, Tatsurokuro
CORPORATE SOURCE: Fac. Agric., Kyoto Univ., Kyoto, 606, Japan
SOURCE: Arch. Biochem. Biophys. (1993), 300(2), 694-8

CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The first enzyme in the formation of GDP-L-fucose from GDP-D-mannose, which forms a GDP-4-keto sugar intermediate, was purified to homogeneity from cell exts. of Klebsiella pneumoniae. During purifn., the enzyme was found to be highly activated by NADP. It was proven that the pyridine nucleotide coenzyme of the enzyme was NADP, not NAD, which differs from previously accepted information. NAD had no effect on enzyme activity. The product of the enzyme reaction with NADP as coenzyme was sepd. from other nucleotides by high-performance liq. chromatog., and using ion spray liq. chromatog./mass spectrometry the mass was detd. for the first time, as 587, which is same as the calcd. mass of GDP-4-keto-6-deoxy-D-mannose.
CC 7-3 (Enzymes)
IT **18186-48-6**, GDP-4-keto-6-deoxy-D-mannose
RL: BIOL (Biological study)
(GDP-mannose dehydratase reaction product of Klebsiella pneumoniae in relation to)

L10 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1990:572456 HCAPLUS
DOCUMENT NUMBER: 113:172456
TITLE: Stereochemistry and mechanism of the GDP-mannose dehydratase reaction
AUTHOR(S): Oths, Philip J.; Mayer, Robert M.; Floss, Heinz G.
CORPORATE SOURCE: Dep. Chem., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Carbohydr. Res. (1990), 198(1), 91-100
CODEN: CRBRAT; ISSN: 0008-6215
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:172456
AB The reaction catalyzed by bacterial GDP-mannose dehydratase (E.C. 4.2.1.47), the conversion of GDP-D-mannose to GDP-4-oxo-6-deoxymannose (GDP-6-deoxy-D-lyxo-hexos-4-ulose), was studied with (6R)- and (6S)-GDP-D-[4-2H1,6-3H]mannose. Conversion of these stereospecifically labeled substrates in the presence of excess unlabeled GDP-mannose into the 4-oxo-6-deoxy derivs. followed by Kuhn-Roth oxidn. gave acetic acid samples which were subjected to configurational anal. of the isotopically chiral Me group. The obsd. F values of 64 for the material from the (6S) substrate and 31 for that from the (6R) isomer, corresponding to 48% e.e. R and 66% e.e. S configuration, resp., of the Me group indicate that (a) the oxidoreductase reaction involves transfer of H(4) to C(6) (b) the transfer is predominantly intramol., and (c) the transfer is stereospecific, H(4) replacing the C(6) hydroxyl group with inversion of configuration. A mechanism for the reaction is proposed on the basis of these results.
CC 33-2 (Carbohydrates)
Section cross-reference(s): 6, 9, 22
IT **18186-48-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, via reaction of GDP-D-mannose with dehydratase, mechanism for)

L16 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:351686 HCAPLUS
DOCUMENT NUMBER: 133:3768
TITLE: Low cost enzymatic biosynthesis of oligosaccharides
INVENTOR(S): Defrees, Shawn; Johnson, Karl
PATENT ASSIGNEE(S): Neose Technologies, Inc., USA
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029603	A2	20000525	WO 1999-US27599	19991118

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 1998-109031	19981118	
US 1998-109096	19981119	

AB This invention provides recombinant cells, reaction mixts., and methods for the enzymic synthesis of saccharides. The recombinant cells contain a heterologous gene that encodes a glycosyltransferase which catalyzes at least one step of the enzymic synthesis, as well a system for generating a nucleotide sugar that can serve as a substrate for the glycosyltransferase. The nucleotide sugar may be supplied or synthesized by an enzymic pathway comprising a sugar nucleotide regeneration cycle. The reaction mixt. may contain a second cell type producing a nucleotide as a substrate for the sugar nucleotide regeneration cycle, preferably by a nucleotide synthase gene. Use of fusion proteins of glycosyltransferase and nucleotide sugar synthase combined with the use of an enzyme for substrate sugar synthesis is described. Chem. or enzymic sulfation may be used for the synthesis of sulfated sugars. The recombinant cells, reaction mixts., and methods are useful for efficiently synthesizing a large variety of saccharides, including polysaccharides, oligosaccharides, glycoproteins and glycolipids, using relatively low-cost starting materials. Synthesis of 3'-sialyllactose using E. coli expressing a CMP-sialic acid synthetase/.alpha.2,3-sialyltransferase fusion protein is described. Optional use of bakers yeast to produce CTP used in the sialic acid cycle and substrate for CMP-sialic acid synthase is also described. Synthesis of 3'-sialyllactose using E. coli expressing a CMP-sialic acid synthetase /.alpha.2,3-sialyltransferase fusion protein, GlcNAc 2'-epimerase, and sialic acid aldolase to synthesize CMP-sialic acid from

GlcNAc is also described. Variations of the method using Corynebacterium expressing a CMP-sialic acid synthetase /.alpha.2,3-sialyltransferase fusion protein and CTP-synthetase to produce the nucleotide, nucleotide sugar, and catalyzing sugar transfer to the acceptor saccharide is described. Finally, synthesis of trisaccharide Gal.alpha.1,3Gal.beta.1,4GlcNAc using Corynebacterium expressing UDP-glucose pyrophosphorylase, UDP-glucose-4'-epimerase, .beta.1,4-galactosyltransferase, and .alpha.1,3-galactosyltransferase is described.

IC ICM C12P
CC 16-4 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 7, 33
IT Azotobacter vinelandii
Bakers' yeast
Corynebacterium
Escherichia coli
Fungi
Plant cell
Prokaryote
Yeast
(host cell for sugar biosynthesis; low cost enzymic biosynthesis of oligosaccharides)
IT 57-48-7, Fructose, biological studies 59-23-4, Galactose, biological studies 63-39-8, UTP 63-42-3, Lactose 65-47-4, CTP 65-86-1, Orotic acid 86-01-1, GTP 127-17-3, biological studies 133-89-1, UDP-glucose 528-04-1 1330-20-7, Xylene, biological studies 1811-31-0, N-Acetylgalactosamine 2616-64-0, UDP-glucuronic acid 2956-16-3, UDP-galactose 3063-71-6 3123-67-9, GDP-mannose 7277-98-7 7512-17-6
15839-70-0, GDP-fucose 50722-58-2, UDP-galacturonic acid
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(low cost enzymic biosynthesis of oligosaccharides)

L16 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:283128 HCAPLUS
DOCUMENT NUMBER: 133:249698
TITLE: A bifunctional **epimerase-reductase** acts downstream of the MUR1 gene product and completes the de novo synthesis of GDP-L-fucose in Arabidopsis
AUTHOR(S): Bonin, Christopher P.; Reiter, Wolf-Dieter
CORPORATE SOURCE: Department of Molecular and Cell Biology, University of Connecticut, Storrs, CT, 06269, USA
SOURCE: Plant J. (2000), 21(5), 445-454
CODEN: PLJUED; ISSN: 0960-7412
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB L-Fucose is a monosaccharide found as a component of glycoproteins and cell wall polysaccharides in higher plants. The MUR1 gene of Arabidopsis thaliana encodes a GDP-D-mannose 4,6-dehydratase catalyzing the first step in the de novo synthesis of GDP-L-fucose from GDP-D-mannose. Plant genes encoding the subsequent steps in L-fucose synthesis (3,5-epimerization and

4-redn.) have not been described previously. Based on sequence similarities to a bacterial gene involved in capsule synthesis we have cloned a gene from Arabidopsis, now designated GER1, which encodes a bifunctional 3,5-epimerase-4-reductase in L-fucose synthesis. The combined action of the MUR1 and GER1 gene products converts GDP-D-mannose to GDP-L-fucose in vitro demonstrating that this entire nucleotide-sugar interconversion pathway could be reconstituted using plant genes expressed in Escherichia coli. In vitro assays indicated that the GER1 protein does not act as a GDP-D-mannose 3,5-epimerase, an enzymic activity involved in the de novo synthesis of GDP-L-galactose and L-ascorbic acid. Similarly, L-ascorbate levels in GER1 antisense plants were unchanged indicating that GDP-D-mannose 3,5-epimerase is encoded by a sep. gene.

CC 11-1 (Plant Biochemistry)
Section cross-reference(s): 3

ST Arabidopsis **epimerase reductase** gene GER1 sequence

IT Gene, plant
RL: PRP (Properties)
(GER1; bifunctional **epimerase-reductase** acts downstream of MUR1 gene product and completes de novo synthesis of GDP-L-fucose in Arabidopsis)

IT Arabidopsis thaliana
DNA sequences
Protein sequences
(bifunctional **epimerase-reductase** acts downstream of MUR1 gene product and completes de novo synthesis of GDP-L-fucose in Arabidopsis)

IT 294220-32-9
RL: PRP (Properties)
(amino acid sequence; bifunctional **epimerase-reductase** acts downstream of MUR1 gene product and completes de novo synthesis of GDP-L-fucose in Arabidopsis)

IT **15839-70-0**, GDP-L-fucose
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(bifunctional **epimerase-reductase** acts downstream of MUR1 gene product and completes de novo synthesis of GDP-L-fucose in Arabidopsis)

IT 113756-18-6, GDP-4-keto-6-deoxymannose **epimerase-reductase**
RL: PRP (Properties)
(bifunctional **epimerase-reductase** acts downstream of MUR1 gene product and completes de novo synthesis of GDP-L-fucose in Arabidopsis)

IT 204024-67-9, GenBank AF045286
RL: PRP (Properties)
(nucleotide sequence; bifunctional **epimerase-reductase** acts downstream of MUR1 gene product and completes de novo synthesis of GDP-L-fucose in Arabidopsis)

REFERENCE COUNT: 37
REFERENCE(S): (1) Altschul, S; J Mol Biol 1990, V215, P403 HCAPLUS
(2) Andrianopoulos, K; J Bacteriol 1998, V180, P998

HCAPLUS
(3) Aoyama, K; Mol Biol Evol 1994, V11, P829 HCAPLUS
(4) Bacic, A; The Biochemistry of Plants 1988, V14, P297 HCAPLUS
(5) Barber, G; Biochem Biophys Acta 1968, V165, P68 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:778579 HCAPLUS
DOCUMENT NUMBER: 130:106887
TITLE: GDP-4-keto-6-deoxy-D-mannose **epimerase/reductase** from Escherichia coli, a key enzyme in the biosynthesis of GDP-L-fucose, displays the structural characteristics of the RED protein homology superfamily
AUTHOR(S): Rizzi, Menico; Tonetti, Michela; Vigevani, Pierpaolo; Sturla, Laura; Bisso, Angela; De Flora, Antonio; Bordo, Domenico; Bolognesi, Martino
CORPORATE SOURCE: Dipartimento di Scienza e Tecnologia del Farmaco, Universita del Piemonte Orientale "A.Avogadro", Novara, 33-28100, Italy
SOURCE: Structure (London) (1998), 6(11), 1453-1465
CODEN: STRUE6; ISSN: 0969-2126
PUBLISHER: Current Biology Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The process of GDP L-fucose (GDP-L-fucose) biosynthesis is conserved throughout evolution from prokaryotes to man. In animals, GDP-L-fucose is the substrate of fucosyltransferases that participate in the biosynthesis and remodeling of glycoconjugates, including ABH blood group and Lewis-system antigens. The "de novo" pathway of GDP-L-fucose biosynthesis from GDP-D-mannose involves a GDP-D-mannose 4,6 dehydratase (GMD) and a GDP-4-keto-6-deoxy-D-mannose epimerase/reductase (GMER). Neither of the catalytic mechanisms nor the three-dimensional structures of the two enzymes has been elucidated yet. The severe leukocyte adhesion deficiency (LAD) type II genetic syndrome is known to result from deficiencies in this de novo pathway. The crystal structures of apo- and holo-GMER have been detd. at 2.1 .ANG. and 2.2 .ANG. resoln., resp. Each subunit of the homodimeric (2 .times. 34 kDa) enzyme is composed of two domains. The N-terminal domain, a six-stranded Rossmann fold, binds NADP+; the C-terminal domain (about 100 residues) displays an .alpha./.beta. topol. NADP+ interacts with residues Arg12 and Arg36 at the adenylic ribose phosphate; moreover, a protein loop based on the Gly-X-X-Gly-X-X-Gly motif (where X is any amino acid) stabilizes binding of the coenzyme diphosphate bridge. The nicotinamide and the connected ribose ring are located close to residues Ser107, Tyr136 and Lys140, the putative GMER active-site center. The GMER fold is reminiscent of that obsd. for UDP-galactose epimerase (UGE) from Escherichia coli. Consideration of the enzyme fold and of its main structural features allows assignment of GMER to the reductase-epimerase-dehydrogenase (RED) enzyme homol. superfamily, to

which short-chain dehydrogenase/reductases (SDRs) also belong. The location of the NADP+ nicotinamide ring at an interdomain cleft is compatible with substrate binding in the C-terminal domain.
CC 7-5 (Enzymes)
ST GDP ketodeoxymannose **epimerase reductase** Escherichia; crystal structure GDP ketodeoxymannose **epimerase reductase**
IT Conformation (protein)
Crystal structure
Escherichia coli
Quaternary structure (protein)
(GDP-4-keto-6-deoxy-D-mannose **epimerase/reductase** (GMER) from Escherichia coli displays structural characteristics of **reductase-epimerase**-dehydrogenase superfamily)
IT Active sites (enzyme)
(NADP+-binding site; GDP-4-keto-6-deoxy-D-mannose **epimerase/reductase** (GMER) from Escherichia coli displays structural characteristics of **reductase-epimerase**-dehydrogenase superfamily)
IT Molecular recognition
(by GMER NADP+-binding site; GDP-4-keto-6-deoxy-D-mannose **epimerase/reductase** (GMER) from Escherichia coli displays structural characteristics of **reductase-epimerase**-dehydrogenase superfamily)
IT Conformation
Molecular structure
(of NADP+ bound to GMER; GDP-4-keto-6-deoxy-D-mannose **epimerase/reductase** (GMER) from Escherichia coli displays structural characteristics of **reductase-epimerase**-dehydrogenase superfamily)
IT 53-59-8D, NADP+, complex with GDP-4-keto-6-deoxy-D-mannose **epimerase/reductase** 113756-18-6, GDP-4-keto-6-deoxy-D-mannose **epimerase/reductase**
RL: PRP (Properties)
(GDP-4-keto-6-deoxy-D-mannose **epimerase/reductase** (GMER) from Escherichia coli displays structural characteristics of **reductase-epimerase**-dehydrogenase superfamily)
IT **15839-70-0**, GDP-L-fucose
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GMER structure in relation to biosynthesis of GDP-L-fucose; GDP-4-keto-6-deoxy-D-mannose **epimerase/reductase** (GMER) from Escherichia coli displays structural characteristics of **reductase-epimerase**-dehydrogenase superfamily)
REFERENCE COUNT: 53
REFERENCE(S): (1) Abeijon, C; Trends Biochem Sci 1997, V22, P203 HCAPLUS
(3) Azzi, A; Nat Struct Biol 1996, V3, P665 HCAPLUS
(4) Baker, M; FEBS Lett 1992, V301, P89 HCAPLUS
(5) Bauer, A; Proteins 1992, V12, P372 HCAPLUS
(6) Bell, C; Protein Sci 1997, V6, P2084 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:237121 HCAPLUS
DOCUMENT NUMBER: 129:64805
TITLE: Molecular cloning of human GDP-mannose 4,6-dehydratase

and reconstitution of GDP-fucose biosynthesis in vitro

AUTHOR(S): Sullivan, Francis X.; Kumar, Ravindra; Kriz, Ronald; Stahl, Mark; Xu, Guang-Yi; Rouse, Jason; Chang, Xiao-jia; Boodhoo, Amechand; Potvin, Barry; Cumming, Dale A.

CORPORATE SOURCE: Small Molecule Drug Discovery, Genetics Institute, Inc., Cambridge, MA, 02140, USA

SOURCE: J. Biol. Chem. (1998), 273(14), 8193-8202
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have cloned the cDNA encoding human GDP-mannose 4,6-dehydratase, the first enzyme in the pathway converting GDP-mannose to GDP-fucose. The message is expressed in all tissues and cell lines examd., and the cDNA complements Lec13, a Chinese Hamster Ovary cell line deficient in GDP-mannose 4,6-dehydratase activity. The human GDP-mannose 4.6-hydratase polypeptide shares 61% identity with the enzyme from Escherichia coli, suggesting broad evolutionary conservation. Purified recombinant enzyme utilizes NADP+ as a cofactor and, like its E. coli counterpart, is inhibited by GDP-fucose, suggesting that this aspect of regulation is also conserved. We have isolated the product of the dehydratase reaction, GDP-4-keto-6-deoxymannose, and confirmed its structure by electrospray ionization-mass spectrometry and high field NMR.

Using purified recombinant human GDP-mannose 4,6-dehydratase and FX protein (GDP-keto-6-deoxymannose 3,5-epimerase, 4-reductase), the authors show that the two proteins alone are sufficient to convert GDP-mannose to GDP-fucose in vitro. This unequivocally demonstrates that the epimerase and reductase activities are on a single polypeptide. Finally, the authors show that the two homologous enzymes from E. coli are sufficient to carry out the same enzymic pathway in bacteria.

CC 7-5 (Enzymes)
Section cross-reference(s): 3, 13

ST human GDP mannose dehydratase sequence cDNA; map gene GDP mannose dehydratase **epimerase**; fucose GDP biosynthesis human cDNA sequence; **reductase epimerase** gene GDP mannose map

IT Human chromosome 8
(8q24.3; **epimerase-reductase** gene mapped on; mol. cloning of human GDP-mannose 4,6-dehydratase and reconstitution of GDP-fucose biosynthesis in vitro)

IT 113756-18-6, GDP-4-keto-6-deoxymannose 3,5-**epimerase** 4-**reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chromosomal mapping of gene for; mol. cloning of human GDP-mannose 4,6-dehydratase and reconstitution of GDP-fucose biosynthesis in vitro)

IT **15839-70-0**, GDP-fucose
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(enzyme inhibition by; mol. cloning of human GDP-mannose 4,6-dehydratase and reconstitution of GDP-fucose biosynthesis in vitro)

L16 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:197631 HCAPLUS
DOCUMENT NUMBER: 128:256472
TITLE: Processes for producing sugar nucleotides and complex carbohydrates
INVENTOR(S): Koizumi, Satoshi; Sasaki, Katsutoshi; Endo, Tetsuo; Tabata, Kazuhiko; Ozaki, Akio
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan; Koizumi, Satoshi; Sasaki, Katsutoshi; Endo, Tetsuo; Tabata, Kazuhiko; Ozaki, Akio
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9812343	A1	19980326	WO 1997-JP3226	19970912
W: AU, BG, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2237849	AA	19980326	CA 1997-2237849	19970912
AU 9742203	A1	19980414	AU 1997-42203	19970912
EP 870841	A1	19981014	EP 1997-940365	19970912
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1207135	A	19990203	CN 1997-191606	19970912
PRIORITY APPLN. INFO.:			JP 1996-244451	19960917
			JP 1996-285066	19961028
			WO 1997-JP3226	19970912

AB Sugar nucleotides are manufd. with microorganism or enzyme producing NTP from nucleotide precursor and with microorganism or enzyme producing sugar nucleotides from sugar and NTP. Complex carbohydrates are manufd. with the described microorganism/enzyme and microorganism/enzyme that produces complex carbohydrates from sugar nucleotide and complex carbohydrate precursor. Also given was prodn. of N-acetylglucosamine-1-phosphate with galactokinase-high microorganism.

IC ICM C12P019-26
ICS C12N001-21; C12N015-54; C12N005-16; C12P019-26; C12R001-19; C12R001-15

CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 33

IT **Corynebacterium**
Corynebacterium ammoniagenes
Escherichia
Escherichia coli
Fermentation
Saccharomyces cerevisiae
Tissue culture (animal)
(processes for producing sugar nucleotides and complex carbohydrates)

IT 133-89-1P, UDP-glucose 528-04-1P 2956-16-3P, UDP-galactose 3063-71-6P 3123-67-9P, GDP-mannose 3554-90-3P 5188-48-7P 6206-28-6P 6614-35-3P 7277-98-7P 13071-22-2P 13117-26-5P

13168-24-6P 13435-89-7P 13551-21-8P 14446-49-2P **15839-70-0P**
, GDP-fucose 20212-77-5P 24656-24-4P 28446-21-1P,
N-Acetylglucosamine-1-phosphate 28447-38-3P 29923-15-7P 34141-02-1P
34621-73-3P 34621-74-4P 34621-93-7P 34621-95-9P 35061-50-8P
35259-23-5P 35954-64-4P 37776-59-3P 39523-49-4P 40592-72-1P
40871-49-6P 52455-62-6P 52630-68-9P 53633-94-6P 55219-45-9P
55637-63-3P 56822-52-7P 56907-30-3P 60283-31-0P 62026-07-7P
67006-44-4P 72506-86-6P 72506-87-7P 76211-71-7P 78151-21-0P
82535-18-0P 95983-78-1P 113890-20-3P 117192-56-0P 136036-84-5P
136198-41-9P 162185-60-6P 205380-69-4P 205380-70-7P 205380-71-8P
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP
(Preparation)
(processes for producing sugar nucleotides and complex carbohydrates)

IT 9001-36-9, Glucokinase 9001-81-4, Phosphoglucomutase 9016-11-9,
Galactose-1-phosphate uridylyltransferase 9023-56-7, CTP synthetase
9026-22-6, Glucose-1-phosphate uridylyltransferase 9026-31-7,
Mannose-1-phosphate guanylyltransferase 9027-60-5 9028-26-6,
UDP-glucose dehydrogenase 9030-08-4, Glucuronosyl transferase
9031-48-5, Glucosyltransferase 9031-68-9, Galactosyltransferase
9033-44-7, Pyrophosphatase 9054-44-8, N-Acetylgalactosaminyl
transferase
9054-49-3, N-Acetylglucosaminyltransferase 9055-06-5,
Mannosyltransferase 9067-82-7 9075-81-4, Sialyltransferase
37211-59-9, GDP-4,6-mannose-dehydratase 37318-34-6 56626-18-7,
Fucosyltransferase 113756-18-6, GDP-4-keto-6-deoxymannose
epimerase-reductase
RL: CAT (Catalyst use); USES (Uses)
(processes for producing sugar nucleotides and complex carbohydrates)

L16 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:681510 HCAPLUS
DOCUMENT NUMBER: 125:321299
TITLE: Synthesis of GDP-L-fucose by the human FX protein
AUTHOR(S): Tonetti, Michela; Sturla, Laura; Bisso, Angela;
Benatti, Umberto; De Flora, Antonio
CORPORATE SOURCE: Inst. Biochem., Univ. Genova, Genoa, 16132, Italy
SOURCE: J. Biol. Chem. (1996), 271(44), 27274-27279
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB FX is a homodimeric NADP(H)-binding protein of 68 kDa, 1st identified in human erythrocytes, from which it was purified to homogeneity. Its function has been unrecognized despite partial structural and genetic characterization. Recently, on the basis of partial amino acid sequence, it proved to be the human homolog of murine protein P35B, a tumor rejection antigen. In order to address the biochem. role of FX, its primary structure was completed by cDNA sequencing. This sequence revealed a significant homol. with many proteins from different organisms.
Specifically, FX showed a marked similarity with a putative Escherichia coli protein, named Yefb, whose gene maps in a region of E. coli chromosome coding for enzymes involved in synthesis and utilization of GDP-D-mannose. Accordingly, a possible role of FX in this metab. was investigated. The data obtained indicated FX as the enzyme responsible for the last step of the major metabolic pathway resulting in GDP-L-fucose
synthesis from GDP-D-mannose in prokaryotic and eukaryotic cells.